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TRIAL DESIGN

Exercise training in patients with a left ventricular assist device (Ex-VAD): rationale and design of a multicentre, prospective, assessor-blinded, randomized, controlled trial

Anna Bobenko[1,2†], Felix Schoenrath[2,4†], Jan H. Knierim[4], Tim Friede[5,6], Nicolas Verheyen[7], Mandeep R. Mehra[8], Mark Haykowsky[9], Christoph Herrmann-Lingen[6,10], André Duvinage[11,12], Elisabeth Pieske-Kraigher[1], Martin Halle[11,12], Volkmar Falk[2,4], Burkert Pieske[1,2,3,13], and Frank Edelmann[1,2,3,6*]

[1]Department of Internal Medicine and Cardiology, Charité University Medicine Berlin, Berlin, Germany; [2]DZHK (German Centre for Cardiovascular Research), Partner Site Berlin, Berlin, Germany; [3]Berlin Institute of Health (BIH), Berlin, Germany; [4]Department of Cardiothoracic Surgery, Deutsches Herzzentrum Berlin (DHZB), Berlin, Germany; [5]Department of Medical Statistics, University Medical Center Göttingen, Göttingen, Germany; [6]DZHK (German Centre for Cardiovascular Research), Partner Site Göttingen, Göttingen, Germany; [7]Department of Cardiology, Medical University of Graz, Graz, Austria; [8]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA; [9]College of Nursing and Health Innovation, University of Texas at Arlington, Arlington, TX, USA; [10]Department of Psychosomatic Medicine and Psychotherapy, University of Göttingen Medical Centre, Göttingen, Germany; [11]Department of Prevention, Rehabilitation and Sports Medicine, Technische Universität München, Munich, Germany; [12]DZHK (German Centre for Cardiovascular Research), Partner Site Munich Heart Alliance, Munich, Germany; and [13]Department of Cardiology, Deutsches Herzzentrum Berlin (DHZB), Berlin, Germany

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Aims Left ventricular assist device (LVAD) therapy is a promising option for patients with advanced heart failure (HF), refractory to guideline-mandated medical treatment either as a bridge to heart transplantation or as lifelong therapy. Functional capacity improves after LVAD implantation but remains reduced in patients with long-term LVAD therapy. Exercise training (ET) improves functional capacity and quality of life (QoL) in HF and may provide incremental benefits in patients supported with LVAD therapy.

Methods The primary objective of Ex-VAD is to investigate whether a 12-week supervised ET can improve peak oxygen uptake ($peakVO_2$) measured by cardiopulmonary exercise testing (CPET) on an ergometer. The study is powered to demonstrate a group difference of 3 mL/min/kg in $peakVO_2$ at week 12, with a power of 0.9 and a standard deviation of 5 mL/min/kg. After baseline assessments to determine whether ET is safe, 66 patients at six trial sites with advanced HF and LVAD therapy will be randomized 2:1 to supervised ET or to the control arm of usual care alone. Patients randomized to ET will perform supervised aerobic endurance and resistance ET (three times/week) for 12 weeks. At baseline and during follow-up, anthropometry, CPET, echocardiography (at rest and exercise), and QoL evaluation will be performed. Blood samples will be collected to examine cardiac-specific relevant biomarkers. Overall physical activity, training sessions, and adherence will be monitored and documented throughout the study using accelerometers and patient diaries.

Conclusions The Ex-VAD trial will assess the effects of a supervised ET programme on $peakVO_2$ and QoL in patients with LVAD. As LVAD therapy moves from crisis support to ambulatory functional enhancement, this trial will provide a rationale to improve functional capacity and, in perspective, cardiovascular outcomes in LVAD-supported patients with advanced HF.

Keywords Advanced heart failure • Left ventricular assist device • Supervised exercise training

*Corresponding author. Charité Universitätsmedizin Berlin, Medizinische Klinik m. S. Kardiologie, Augustenburger Platz 1, 13353 Berlin, Germany. Tel: +49 30 450 653 731, Fax: +49 30 450 755 3731, Email: frank.edelmann@charite.de

[†]These authors contributed equally to first authorship. [Affiliation [4] added for Felix Schoenrath on 17 April 2019, after first online publication.]

Introduction

Evidence-based therapies have improved survival in chronic heart failure (HF).[1] However, patients still progress to advanced stage of HF.[2,3] Left ventricular assist device (LVAD) therapy may improve outcome in advanced HF[4] and has transitioned from initially life-saving therapy for patients ineligible for heart transplantation to destination therapy.[3] However, after LVAD implantation, functional capacity measured objectively as peak oxygen uptake (peakVO_2) and quality of life (QoL) improves but still remains limited compared to normals.[5–9]

Exercise training (ET) is a safe and effective treatment modality in HF, it significantly improves exercise capacity, QoL and HF signs and symptoms, and has benefit on morbidity, mortality and hospitalization as demonstrated in previous multicentre randomized controlled trials.[10,11] Therefore, it is recommended in current guidelines for chronic HF.[1,12]

Several small single-centre randomized ET intervention trials have previously been conducted in advanced HF patients treated by LVAD therapy.[13–16] These trials demonstrated that ET is feasible, safe and tends to improve maximal and submaximal exercise capacity (peakVO_2, 6 min walk distance), muscle strength and QoL in patients with LVAD. However, due to low sample sizes, low number of training sessions and short intervention periods, these trials showed conflicting results with ET. Overall, data on ET in LVAD are rare.[16]

Data from the Ex-DHF pilot trial with 12 weeks of ET in chronic HF patients and the the exercise intervention trial by Laoutaris *et al.*[17,18] support the notion that aerobic training with a higher number of training sessions on a larger sample size of patients than previously tested might have beneficial effects in advanced HF patients with LVAD therapy. In a case study we demonstrated safety and efficacy of our ET in a patient with LVAD and showed marked improvement of peakVO_2 from 9.7 mL/min/kg to 15.3 mL/min/kg in 12 weeks.[19]

Therefore, the 'Exercise training in patients with left ventricular assist device' (Ex-VAD) trial was designed to evaluate the effects of supervised ET on functional capacity in patients with LVAD. We will test the hypothesis that 12 weeks of supervised ET improves peakVO_2 in a multicentre setting.

Study design

The primary objective of the Ex-VAD trial is to determine whether supervised ET is superior to usual care alone in improving peakVO_2 in patients with advanced HF and LVAD therapy.

As secondary objectives, the Ex-VAD trial also evaluates whether ET improves submaximal exercise capacity, muscle strength, QoL, echocardiographic parameters of systolic and diastolic function at rest and during exercise, left ventricular geometry and dimensions, and markers of neurohumoral activation. Change in body composition, cognition, frailty and daily physical activity will be evaluated. Safety and feasibility of ET will be assessed.

Trial population

The Ex-VAD trial aims to enrol 66 stable patients with advanced chronic HF and LVAD support and therapeutic treatment according to the European Society of Cardiology HF guidelines.[1] A pre-defined set of inclusion and exclusion criteria (*Table 1*) was selected to ensure feasibility and safety of ET and all stress tests during the trial and to minimize the number of patients discontinuing the intervention or the study prematurely.

Briefly, inclusion criteria are stable advanced HF at least 3 months post-LVAD implantation, absence of acute illness prohibiting exercise, and optimal pharmacologic therapy for 4 weeks before enrolment is strongly advocated. Patients should be able to perform cardiopulmonary exercise testing (CPET) at least 1 min at 20 W and may perform any kind of leisure time physical activity.

Key assessments

Cardiopulmonary exercise testing

Before randomization, CPET will be performed to determine whether patients can exercise safely, including blood pressure response, ischaemic changes, and significant arrhythmias as recommended by international guidelines.[12] Symptom-limited CPET is performed using a bicycle ergometer with the initial workload of 20 W and increased by 10 W every minute. PeakVO_2 is defined as the highest oxygen uptake value of the last 30 s before termination of exercise using 10 s-averaged values. CPET is repeated 12 and 24 weeks after randomization for all patients. All data are blinded for intervention group and time point of assessment will be forwarded to an assessor-blinded CPET core lab to ensure good data quality (e.g. based on peak respiratory exchange ratio, peak heart rate). The core lab trains and certifies all investigators performing CPET prior to start of recruitment.

Echocardiography

Echocardiographic images and loops will be digitally recorded and stored on site and will be analysed in an assessor-blinded reference echocardiography core lab. All images from parasternal, apical and subcostal views are obtained based on standard views as described in the guidelines of the American Society of Echocardiography.[20–22] At baseline resting and stress echocardiography with dobutamine are performed to assess systolic and diastolic function and to rule out other cardiac disease that may influence exercise capacity, e.g. severe valvular disease or intracardiac thrombus. Echocardiography is repeated 12 and 24 weeks after randomization.

Laboratory measurements and biobanking

Blood samples will be taken in standardized conditions after at least 5 min resting position, and urine samples will be collected from fresh midstream urine. All samples will be immediately centrifuged, aliquoted and stored at −80°C according to the standard operating procedure. Local blood and urine analysis will be performed in a local certified laboratory.

Table 1 Inclusion and exclusion criteria of the Ex-VAD trial

Inclusion criteria

- Age ≥ 18 years
- Chronic end-stage systolic heart failure
- Stable on left ventricular assist device, meaning:
  - No major change in therapeutic regime within past 4 weeks: no new additional disease-modifying drug (angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, sacubitril, beta-blocker), no change in disease-modifying drug dosage more than 50% (excluded: diuretics), no initiation of cardiac rehabilitation for a minimum of 4 weeks
  - Post implantation ≥3 months
  - Expected further period on the device for a minimum of 3 months after recruitment into the study
- Ability to complete the study in compliance with the protocol.
- General ability of the patient to declare willingness to participate in the trial.
- Written informed consent

Exclusion criteria

- Acute illness that does not allow exercise, including unstable heart failure, acute myocarditis, acute pericarditis, stroke
- Untreated life-threatening cardiac arrhythmias
- Uncontrolled hypertension
- Intracardiac thrombus
- Inability to perform cardiopulmonary exercise testing at least 1 min at 20 W
- Uncontrolled diabetes
- Uncontrolled kidney disease
- Recent embolism
- Concurrent, continuous, or intermittent dobutamine therapy
- Complex ventricular arrhythmia at rest or appearing with exertion
- Supine resting heart rate > 100 b.p.m.
- Severe pulmonary instability
- Haemodynamically relevant valvular disorders
- Significant change in cardiovascular medication within the previous 4 weeks (see inclusion criteria)
- Severe anaemia (haemoglobin < 8 g/dL), however patients with moderate anaemia (haemoglobin < 11 g/dL) may be recruited if clinically stable (investigator assessment)
- Clinically relevant musculoskeletal disease

Psychometric analysis

Quality of life will be assessed at baseline using a set of standardized validated questionnaires and repeated 12 and 24 weeks after randomization for all patients. Analysis will be assessor-blinded and performed using objective algorithms by a QoL core lab.

Randomization

After informed consent and screening, patients are randomized in a 2:1 ratio to either ET or usual care alone. The randomization is carried out using a central computerized only system of the German Centre for Cardiovascular Research (DZHK). The randomization procedure is a block randomization stratified by centre and indication for LVAD (bridging vs. destination therapy). The allocation is concealed to staff and patients. A study flow chart is shown in *Figure 1*.

Usual care

The Ex-VAD trial efforts to ensure that patients are already receiving appropriate and stable guideline-based care prior to entering the trial. Also, during the duration of the trial, patients will continue to be monitored by their LVAD physician; changes in medication and pump settings will be recorded throughout the trial.

Patients of both treatment groups will receive the same number of visits throughout the trial. All patients will be examined at baseline, 12 and 24 weeks after randomization. Examination will include medical history, physical examination, anthropometry, biochemical analysis, electrocardiogram (ECG), resting and dobutamine stress echocardiography, submaximal exercise capacity (6 min walk test), CPET (peakVO_2), muscle strength and body composition assessment, and multiple validated self-reporting questionnaires assessing physical activity, exercise motivation, self-efficacy, QoL and distress. In addition, 2, 4, 8 and 16 weeks after randomization, safety visits will take place. At these visits, physical examination, biochemical analysis and ECG will be performed to ensure patient safety during the trial.

All patients will be advised to follow their daily leisure time physical activity as usual. Since daily activity is an important co-variable, it will therefore be continuously recorded using the MotionWatch 8 actigraphy system (CamNtech, Cambridge, UK) and patient diaries.

Exercise training intervention

Patients randomized to ET will perform 36 supervised training sessions consisting of combined pre-defined endurance and resistance training three times per week for 12 weeks on top of usual care. Also, patients will regularly be encouraged to be physically active on the other days. The training is a combination of both endurance and resistance training, based on the Ex-DHF pilot study.[17] The basic training plan for the Ex-VAD trial is summarized in *Table 2*.

Endurance training

The first 4 weeks of training will be exclusively cycle ET. At baseline, exercise intensity of endurance training will be determined by CPET. Patients will start with 20 min of training at 80–100% of anaerobic threshold (determined by CPET) and the duration will increase to 60 min after 3 months (*Table 2*). The 'aerobic training phase' will be preceded and followed by a 5 min warm-up and 5 min cool-down, respectively. During ET, intensity of training will be monitored through workload (W) and Borg scale and will be increased during 3 months of ET.

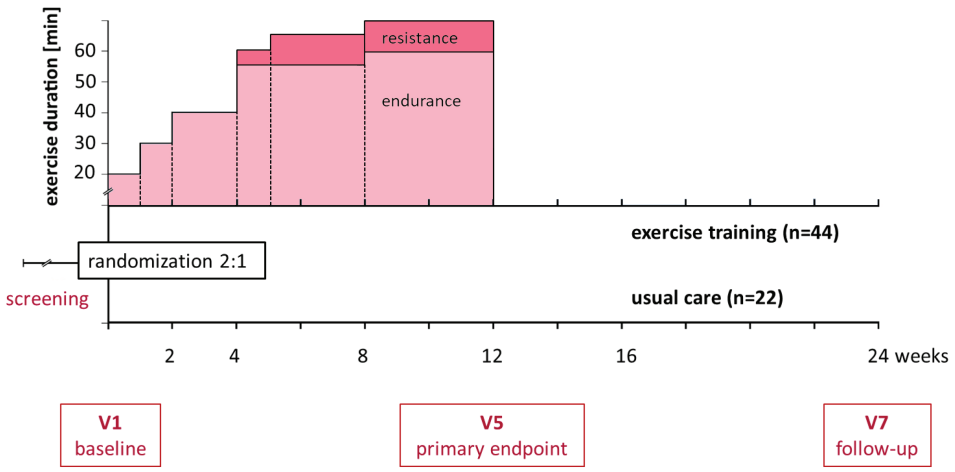

Figure 1 Flow chart of the Ex-VAD trial. After screening, patients are randomized 2:1 at baseline visit to either exercise training (including endurance and resistance training) on top of usual care or usual care alone. Visits are scheduled at 2, 4, 8, 12, 16 and 24 weeks after randomization. Duration and intensity of supervised exercise training are increased stepwise. The primary endpoint is determined after 12 weeks (V5).

Table 2 Schedule of the exercise training intervention

		Endurance training (3 per week)			Resistance training (3 per week)				
Phase	**Week**	**Duration (min)[a]**	**Borg (6–20)**	**%Watt @VT1**	**% 1-RM upper extremities**	**% 1-RM lower extremities**	**Set**	**Repetition**	**Free exercises flexibility, balance, coordination (number or exercises)**
1	1	20	12	80–100					6
2	2	30	13	80–100					10
3	3–4	40	14						10
4	5	55	14		10	30	1	10	10
5	6–8	55	15		20	40	2	12	10
6	8–12	60	15		30	50	2	15	10

VT1, anaerobic threshold; 1-RM, one repetition maximum (determined at first training session at week 5).
[a]Duration of endurance training + warm-up and cool-down.

Resistance training

After initial 4 weeks, a tailored resistance training will be added to the endurance training. The intensity of resistance training will be determined through multiple repetition maximum[23] testing at week 4 to predict the one repetition maximum (1-RM). Target intensities will be 10–30% of 1-RM for upper extremities and 30–50% of 1-RM for lower extremities. Resistance training will consist of large muscle group exercises. For each exercise, 10–15 repetitions will be performed.

Free exercises

In addition to endurance and resistance training, an individual set of 6–10 free exercises will be performed to improve flexibility, balance and coordination.

Adherence

Adherence refers to the degree to which trial participants comply with the intervention protocol. In the Ex-VAD trial, this is expected to be challenging due to the highly complex patient population and to the high frequency of the ET intervention. Patients need to complete at least 66% of the possible supervised training sessions to be considered on-treatment.

The Ex-VAD trial uses several approaches to promote adherence. First, patients randomized to ET will regularly be encouraged to attend supervised training sessions by the investigator and by the trainer. All patients will be encouraged to engage in leisure time physical activity by the investigator. Training attendance diaries will be used to monitor adherence of all participants throughout the trial.

Table 3 Secondary endpoints

- Change in ventilatory efficacy (VE/VCO_2 slope) and submaximal exercise tolerance (6 min walk distance, anaerobic threshold) after 3 and 6 months
- Change in muscle strength after 3 and 6 months (e.g. assessed by handgrip)
- Change in body composition after 3 and 6 months
- Change in quality of life (e.g. KCCQ, SF-36) after 3 and 6 months
- Change in cognition after 3 and 6 months
- Change in echocardiographic parameters of cardiac (right and left heart) morphology and function at rest and during exercise after 3 and 6 months: e.g. left ventricular ejection fraction, left ventricular end-diastolic volume and diameters, systolic wall motion peak velocity (S_{max}), TAPSE, fractional area change, peak systolic velocity of tricuspid valve annulus
- Change in markers of neuroendocrine activation (e.g. NT-proBNP), inflammation, collagen turnover and fibrosis as well as metabolic parameters after 3 and 6 months
- Frailty in LVAD and its interaction with exercise training
- Long-term effects of exercise training (6 months)
- Change in daily physical activity
- Adherence to exercise training
- Safety and tolerability of training intervention

KCCQ, Kansas City Cardiomyopathy Questionnaire; LVAD, left ventricular assist device; NT-proBNP, N-terminal pro-B-type natriuretic peptide; SF-36, 36-Item Short-Form Health Survey; TAPSE, tricuspid annular plane systolic excursion.

Endpoints

The primary endpoint for the Ex-VAD trial is change in $peakVO_2$ after 12 weeks. Secondary endpoints include submaximal exercise capacity, echocardiographic parameters of left and right ventricular geometry and dimensions (at rest and during dobutamine stress echocardiography), diastolic and systolic function, body composition, frailty, QoL, and markers of neuroendocrine activation (*Table 3*). Safety, tolerability and adherence to ET intervention will be assessed.

Statistical analysis

Based on findings of the Ex-DHF pilot study,[17] we assume a group difference of 3 mL/min/kg in $peakVO_2$ at week 12, a standard deviation of 5 mL/min/kg for $peakVO_2$ at week 12, and a correlation of 0.8 between the measurements at baseline and week 12. Under these assumptions, a total sample size of 51 patients with 2:1 randomization (34 patients in the exercise group, 17 patients in the control group) provides a power of 0.9 for a comparison of group means at the one-sided significance level of 2.5% in an analysis of covariance with baseline adjustment. Previous studies on ET in advanced HF patients with LVAD therapy only reported small numbers of dropouts during the active study period.[13,14] However, considering the extended duration of training of 3 months, we took a conservative approach accounting for a dropout rate of 20%.

Accounting for dropout of about 20%, we aim to recruit a total of 66 patients (44 patients in the exercise group, 22 patients in the control group). The sample size calculation was carried out using nQuery Advisor 7.0. Assumptions regarding the variability of the outcome and the dropout rate will be checked in a blinded sample size review.[24]

The primary endpoint will be analysed by means of a Gaussian linear model for repeated measures with treatment group (exercise vs. control), study centre, indication for LVAD implantation (bridging vs. destination therapy), time and treatment-by-time interaction as factors, and baseline $peakVO_2$ as covariate, including all patients with at least one post-baseline measurement. The error terms are assumed to follow a multivariate normal distribution with unstructured covariance. Least squares mean changes from baseline will be reported for both groups with 95% confidence interval (CI) as well as the difference between the least squares treatment group means with 95% CI and two-sided *P*-value testing the null hypothesis of no treatment effect. Although the model described above is robust to a certain extent to missing data, sensitivity analyses will be performed as supporting analyses including multiple imputation to investigate the sensitivity of the results to missing data assumptions.[25]

The analyses of QoL scales, echocardiographic parameters, biomarkers as well as the other CPET parameters will follow the same lines as the primary analysis outlined above. This model will also be used to investigate the sustainability of the intervention effect over 24 weeks. In further analyses, gender and device type differences will be investigated. For this purpose, gender or device type as well as its interaction with treatment will be included as additional factors in the Gaussian linear model described above. For safety analysis, adverse events will be summarized as frequencies and percentages by treatment group. If a sufficient number of events occur, survival will be analysed by Kaplan–Meier curves stratified by treatment group and differences in survival will be tested using a log-rank test. Recurrent hospitalizations will be modelled by negative binomial regression, a regression model appropriate for recurrent events accounting for between-patient heterogeneity.[26] The analyses of the secondary and safety endpoints have an exploratory character and will therefore not be adjusted for multiple testing.

Trial organization

The Principal Investigator, the Study Coordinator and the Coordination Centre for Clinical Trials Leipzig are responsible for all aspects of the study protocol and amendments. The Steering Committee guarantees scientific oversight and consulting in all study-related aspects. Additional scientific input is provided by an external advisory board, which acts in close collaboration with the Steering Committee. The Data Safety Monitoring Board (DSMB) operates independently of the other study committees and of the sponsor. The DSMB reviews the progress of the trial and, under blinded conditions, controls the safety of the patients enrolled in the Ex-VAD trial. Before enrolling patients, the protocol was

approved by the relevant institutional review boards, research ethics boards, and ethics committees of all the participating centres and the Coordination Centre.

The clinical trial is conducted in accordance with local laws and ICH guidelines for good clinical practice issued in June 1996 and CPMP/ICH/135/95 from September 1997 taking into account the Declaration of Helsinki and all its revisions. The study has been approved by the Regional Committees for Medical Research Ethics of all participating centres (EA2/165/17). The study was registered at https://clinicaltrials.gov; the registration number is NCT03369938. The trial started in December 2017 and is currently recruiting.

Discussion

The Ex-VAD trial is a randomized controlled trial of ET in patients with advanced HF and LVAD therapy. This trial is the first adequately powered study, conducted at multiple centres and comprehensively designed to evaluate the clinical effectiveness of ET in this special population of LVAD implanted patients with advanced HF.

Previous multicentre studies have demonstrated that ET improves exercise capacity and QoL in patients with HF and has beneficial effect on mortality and hospitalization rate.[10,11] The HF-ACTION trial showed a change in peakVO_2 of 0.6 mL/min/kg in the exercise group within 3 months of training vs. 0.2 mL/min/kg in the control group.[10] This significant effect was achieved by supervised aerobic training alone in a cohort of HF patients. The single centre trial by Bouchla *et al.*[27] demonstrated a beneficial effect of adding muscle strength training in HF patients. Combined aerobic and muscle training achieved an additional increase in peakVO_2 of 1.0 mL/min/kg within 3 months of training compared to aerobic training alone.[27] Laoutaris *et al.*[18] investigated the effects of combined aerobic, muscle and inspiratory training and confirmed these results. Interestingly, Laoutaris *et al.*[18] showed a significant increase in left ventricular ejection fraction after 3 months of ET in HF patients with reduced left ventricular ejection fraction.

Three small single-centre randomized controlled trials showed promising results for ET also in LVAD. Kerrigan *et al.*[13] included patients after recent LVAD implantation into 6 weeks of supervised ET vs. control. Hayes *et al.*[14] conducted a similar programme with 8 weeks of supervised ET vs. control. Although peakVO_2 increased in the ET group of both trials, between-group differences were not statistically significant. This may be due to small sample size, short intervention period, and short time post-implantation.

In a randomized trial conducted by Laoutaris *et al.*,[15] the intervention group presented with a significant increase in peakVO_2 after 10 weeks of aerobic training when compared to the control group. Since the trial was published in 2011, most patients were supported by pulsatile-flow LVAD, which is no longer state of the art.

At present, data on ET in LVAD are scarce.[16,28] From the few published trials, none has investigated differences in indication (bridging vs. destination therapy), duration from LVAD implantation to start of ET, or impact of pump settings on ET under controlled conditions. Underlying disease leading to LVAD implantation, indication and co-morbidities have often not been reported in previous trials.[16] Also, due to small sample sizes and predominately male patients receiving LVAD support, gender differences have not been assessed.

The investigators opted for a 2:1 allocation in favour of the intervention group as this is attractive to patients and investigators alike and therefore may help recruitment. Compared to the usual 1:1 allocation, the sample size increases by 12.5% which appears reasonable given the obvious advantages.[29] As blinding of patients and treating health professionals is not feasible with the exercise intervention, a so-called prospective randomized open blinded endpoint (PROBE) design is used. Allocation concealment and blinded endpoint assessment with regard to CPET and echocardiography are crucial here to minimize the risk of bias.

The training programme for the Ex-VAD trial has been previously shown to be feasible and safe, and achieved high adherence in patients with HF with preserved ejection fraction.[17] It has also been tested in a LVAD case study.[19] Given the current guidelines on exercise in HF,[1] it would be unethical not to recommend any physical activity to our patients. Therefore, all patients of the Ex-VAD trial will be encouraged to be physically active in their leisure time. The Ex-VAD investigators recognize that patients in the usual care arm will not have the potential benefit of interacting with exercise trainers, which patients of the ET arm have during supervised training sessions.

Feasibility of supervised training and attendance will be critically evaluated during the Ex-VAD trial. To implement ET as a standard therapy for LVAD, a translation of ET into clinical practice must be made possible. Endurance training is easy to perform and the chosen resistance training exercises on weight-lifting machines are classical and can be performed on regular fitness centre equipment. Also, monitoring by Borg scale is easy to learn and CPET is done regularly in medical centres. Therefore, translation into clinical practice should be feasible, making ET a promising therapy option for LVAD patients.

Since adherence is a substantial factor for ET to successfully improve exercise capacity, several psychological constructs are included to evaluate adherence barriers. In addition, we will investigate whether there are patient subgroups that might benefit from ET more than others. Several mechanisms may contribute to the effect of ET in LVAD: improvement in central cardiac function,[17,30] improvement in respiratory muscle function,[15,18,31] increase in local blood and metabolic activity of skeletal muscle,[32,33] improvement of peripheral oxygen utilization, change in mitochondrial energy metabolism,[34] as well as combinations of these mechanisms. Sub-studies of the Ex-VAD trial will therefore assess the effects of ET on inflammatory markers,[30] metabolic parameters,[35] collagen turnover, frailty,[36] and novel non-standard echocardiographic parameters of systolic and diastolic function.

The Ex-VAD investigators strongly believe that with this trial, functional outcomes from LVAD therapy may be further improved. Due to reduced functional capacity and frequent rehospitalizations, LVAD patients are often impaired in their daily activities and excluded from employment. If a structured supervised ET improves these parameters, the enhancements to function and QoL may encourage greater incorporation and participation within community and societal activities.

Summary

The Ex-VAD trial will assess the effects of a supervised ET programme on functional capacity in patients with LVAD. This trial can provide a rationale to improve functional capacity and, prospectively, cardiovascular outcomes in LVAD-supported patients with advanced HF.

Funding

The trial is financially supported by the German Centre for Cardiovascular Research (Deutsches Zentrum für Herz-Kreislauf-Foschung, DZHK.

Conflict of interest: T.F. has received personal fees for consultancies (including data monitoring committees) in the past 3 years from Bayer, Biosense Webster, Boehringer Ingelheim, Daiichi Sankyo, Feldmann Patent Attorneys, Galapagos, Grünenthal, Janssen, Mediconomics, Novartis, Penumbra, Roche, SGS; all outside the submitted work. M.R.M. declares consulting relationships with Abbott, Medtronic, Janssen, Mesoblast, Portola, Bayer and NupulseCV, Inc. M.H. holds the Moritz Chair in Geriatrics in the College of Nursing and Health Innovation at the University of Texas at Arlington. The other authors have no conflicts of interest.

Appendix

Ex-VAD Trial Investigators and Committees

Principal investigator: Frank Edelmann

Co-Principal investigators: Burkert Pieske, Martin Halle, Volkmar Falk

Steering Committee: Frank Edelmann, Burkert Pieske, Volkmar Falk, Martin Halle, Bernd Wolfarth, Nicolas Verheyen, Anna Bobenko, Tim Friede

Endpoint Committee: Marcus Dörr, Stephan von Haehling, Stefan Störk

Data Safety Monitoring Board: Stefan Felix, Karl Wegscheider, Karl-Ludwig Laugwitz

Trial statistician: Tim Friede

External Advisory Board: Mandeep R. Mehra, Mark Haykowsky

Study Coordination: Anna Bobenko

Project Management: Doris Bach and ZKS Leipzig

Data Management: German Centre for Cardiovascular Research (DZHK), Thomas Franke

Monitoring: ZKS Leipzig

Sponsor: Charité Universitätsmedizin Berlin

Basis Biobanking: Matthias Nauck

Reference centres: Frank Edelmann/Anna Bobenko (CPET); Martin Halle (Exercise training); Elisabeth Pieske-Kraigher (Echocardiography); Christoph Herrmann-Lingen (Psychometric Analysis).

Trial sites: Frank Edelmann, Burkert Pieske, Volkmar Falk (Berlin); Martin Halle, Heribert Schunkert, Rüdinger Lange, Steffen Massberg, Christan Hagl, André Duvinage (München); Stefan Blankenberg, Hermann Reichenspurner, Dirk Westermann, Meike Rybczynski (Hamburg); Ralf Westenfeld (Düsseldorf); Michael Borger, Sandra Eifert (Leipzig); Torsten Doenst, Gloria Färber (Jena).

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